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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/610,891	07/06/00	MCARTHUR J	40567

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1642	8

DATE MAILED: 08/29/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary	Application No.	Applicant(s)	
	09/610,891	MCARTHUR ET AL.	
	Examiner	Art Unit	
	Natalie A. Davis	1642	

-- The MAILING DATE of this communication appears on the cover sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 June 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

Applicant's amendment filed 25 June 2001 (Paper No. 6) is acknowledged. Accordingly, claims 1-22 are cancelled and claims 23-34 added. Claims 23-34 are being examined.

Information Disclosure Statement

The information disclosure statement filed 25 June 2001 has been considered. A signed copy is attached hereto.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 23-34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir., 1988). They include: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The elected claims are drawn to a vaccine comprising a nucleic acid encoding a tumor-associated antigen, wherein tumor associated antigen does not stimulate a humoral response, but stimulates a response when exposed on a proliferation-incompetent cell in the presence of a cytokine. The claims are further drawn to an autologous and allogenic proliferation-incompetent

cell, a cytokine expressed by a second noncancerous cell, the GM-CSF cytokine, and a prostrate proliferation-incompetent cell. The claims are further drawn to a host cell comprising said nucleic acid, wherein the antigen is on the surface of the cell and further comprises a nucleic acid encoding a cytokine and further comprising a second cell comprising a nucleic acid comprising a cytokine.

3. The specification disclose that vaccine treatment enables the immune system of the patient to recognize a tumor-associated antigen thus, overcoming immune tolerance to the antigen, which may suppress tumor growth and lead to the eradication of the tumor (page 24). The specification, further disclose that patients with progressive, micrometastatic prostrate cancer, underwent surgery with appropriate concomitant medications, were given the claimed vaccine, and intradermal sites biopsied. The biopsy sites displayed distinctive inflammatory infiltrate, composed of macrophages, dendritic cells, eosinophils, and T-cells. Furthermore, patients displayed DTH reactivity and reduced PSA serum levels (page 61-63).

4. The instant disclosure fails to meet the enablement requirement for the following reasons:

The specification does not provide any guidance or exemplify that the claimed vaccine induces protective immunity against prostrate or any cancer. The specification indicates that the vaccine stimulates a humoral response, but does not give any definitive evidence that the humoral response is able to protect a patient from developing cancer. The fact that an agent is able to stimulate a humoral response does not necessarily mean that it is capable of generating the immunoprotective response needed to fulfill the definition of a vaccine. The disclosure does not give any definitive evidence that the vaccine or the surgery and concomitant medications were responsible for the decrease in PSA serum levels. Furthermore, there is no guidance or exemplification that the vaccine is able to prevent tumor recurrence and to eliminate residual disease.

7. Articles by Ezzell (J. NIH Res, 1995, 7:46-49) and Spitler (Cancer Biotherapy, 1995, 10:1-3) are cited in order to establish the general state of the art and the level of predictability of vaccines. Ezzell reviews the current thinking in cancer vaccines and states that tumor

immunologists are reluctant to place bets on which cancer vaccine approach will prove effective in the long run and further states that no one is very optimistic that a single peptide will trigger an immune response strong enough to eradicate tumors or even to prevent the later growth of micrometastases among patients whose tumors have been surgically removed or killed by radiation or chemotherapy (page 48, para 6). In addition, Spitler recognizes the lack of predictability of the nature of the art when she states that "Ask practicing oncologists what they think about cancer vaccines and you're likely to get the following response: "cancer vaccines don't work." Ask a venture capitalist or the director of product development at a large pharmaceutical company and you're likely to get the same response" (page 1, para 1).

8. The art teaches that the efficacy of therapeutics is dependent upon factors such as solubility of the drug, bioavailability at the target site, attainment of effective plasma concentrations, solubility in tissues, biotransformation, toxicity, proteolytic degradation, immunological inactivation, rate of excretion or clearance (half-life), deactivation by the liver, hydrolysis in serum, binding to plasma protein, and in the case of antivirals, propensity for emergence of resistant strains (see Benet et al., pp. 3-32, in The Pharmacological Basis of Therapeutics, 8th ed., 1990, page 3, first paragraph; page 5, second column, last partial paragraph, first two sentences; page 10, the paragraph bridging columns 1 and 2; page 18, the paragraph bridging columns 1 and 2; page 20, last full paragraph; and the paragraph bridging pages 20 and 21 and footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO BD> APP>& Inter. 1992). Therefore, in view of the lack of predictability of the prior art and the absence of working examples, it would require undue experimentation for one skilled in the art to practice the invention as claimed.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

10. Claim 23-34 rejected under 35 U.S.C. 102(b) as being anticipated by Dranoff, et al. (6,637,483, 1997). The elected claims are drawn to a vaccine comprising a nucleic acid encoding a tumor-associated antigen, wherein tumor associated antigen does not stimulate a humoral response, but stimulates a response when exposed on a proliferation-incompetent cell in the presence of a cytokine. The claims are further drawn to an autologous and allogenic proliferation-incompetent cell, a cytokine expressed by a second noncancerous cell, the GM-CSF cytokine, and a prostrate proliferation-incompetent cell. The claims are further drawn to a host cell comprising said nucleic acid, wherein the antigen is on the surface of the cell and further comprises a nucleic acid encoding a cytokine and further comprising a second cell comprising a nucleic acid comprising a cytokine.

Dranoff, et al. teach irradiated tumor cell vaccines engineered to express GM-CSF. These vaccines comprise tumor cells, wherein tumor antigens are expressed on the surface and is rendered proliferation incompetent due to irradiation of the cells and genetically engineered cells, which produce GM-CSF and other cytokines. The vaccine may also, comprise a single cell that expresses both the tumor antigen and the cytokine. It is inherent that the cells may be allogenic or autologous, as both cell types are capable of expressing tumor-associated antigens that the proliferation-incompetent cell may be a prostrate cell, as it is capable of expressing a tumor-associated antigen that will not cross-react with prostrate specific antigen. It is also inherent that antigens will have the molecular weights as claimed as cells may express antigens of various molecular weights or may be engineered to do so. Thus, the prior art reference teaches the vaccine as claimed.

11. Claims 23-29 and 30-34 are rejected under 35 U.S.C. 102(a) as being anticipated by Hiserdodt, et al., (WO 98/04282, 1998). The elected claims are drawn to a vaccine comprising a nucleic acid encoding a tumor-associated antigen, wherein tumor associated antigen does not stimulate a humoral response, but stimulates a response when exposed on a proliferation-incompetent cell in the presence of a cytokine. The claims are further drawn to an autologous and allogenic proliferation-incompetent cell, a cytokine expressed by a second noncancerous

cell, the GM-CSF cytokine, and a prostrate proliferation-incompetent cell. The claims are further drawn to a host cell comprising said nucleic acid, wherein the antigen is on the surface of the cell and further comprises a nucleic acid encoding a cytokine and further comprising a second cell comprising a nucleic acid comprising a cytokine.

Hiserdodt, et al. teach a vaccine comprising nucleic acids encoding a tumor-associated antigen on a proliferation-incompetent cell, which may be allogenic, autologous, and a prostrate cell, it further comprises a cytokine producing cell, which stimulates the tumor-associated to respond humorally and wherein the cytokine is GM-CSF. Hiserdodt, et al. further teach a vaccine comprising host cell comprising a nucleic acid encoding a cytokine, which is GM-CSF, a vaccine further comprising a second cell comprising a nucleic acid encoding a cytokine, which is GM-CSF (pages 7-9, 12-13,15-18, 20, 23). Thus, the prior art reference teaches the vaccine as claimed.

12. No claims allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Natalie A. Davis whose telephone number is 703-308-6410. The examiner can normally be reached on M-F 8-5:30 (every other Friday off).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4315 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Natalie A. Davis, Ph.D.
August 23, 2001

ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Attachment for PTO-948 (Rev. 03/01, or earlier)
6/18/01

The below text replaces the pre-printed text under the heading, "Information on How to Effect Drawing Changes," on the back of the PTO-948 (Rev. 03/01, or earlier) form.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

1. Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings MUST be filed within the THREE MONTH shortened statutory period set for reply in the Notice of Allowability. Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136(a) or (b) for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

2. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, MUST be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings MUST be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit the drawing corrections within the time period set in the attached Office communication. See 37 CFR 1.85(a).

Failure to take corrective action within the set period will result in ABANDONMENT of the application.